AMENDMENT

A Version With Markings to Show Changes Made is included after Applicant's Remarks.

In the Specification:

Please delete the paragraph at page 4, lines 11-17, and insert therefor the following:

--Intracarotid infusion of leukotriene C_4 (LTC_4) selectively increases the permeability in brain tumor capillaries without affecting the permeability in normal brain capillaries. The effect of LTC_4 on brain tumor capillaries is, however, limited to small molecules and it can only slightly increase the permeability of those small molecules in abnormal brain tissue relative to normal. Accordingly, LTC_4 does not significantly increase the delivery of some larger water soluble molecules to brain tumors or other abnormalities.--.

Please delete the paragraph at page 4, line 18 through page 5, line 3, and insert therefor the following:

--The vasoactive nonopeptide bradykinin and agonists or polypeptide analogs thereof (e.g., receptor-mediated permeabilizers [RMPs]) have been injected intravenously to increase blood-brain barrier permeability to co-administered neuropharmaceutical or diagnostic agents. (B. Malfroy-Camine, *Method for increasing blood-brain barrier permeability by administering a bradykinin agonist of blood-brain barrier permeability*, U.S. Patent No. 5,112,596; J.W. Kozarich *et al.*, *Increasing blood brain barrier permeability with permeabilizer peptides*, U.S. Patent No. 5,268,164). Intracarotid infusion of bradykinin will selectively increase permeability 2- to 12-fold in brain tumor and ischemic brain capillaries for molecules ranging in molecular weight from 100 to 70,000 Daltons (Inamura, T. *et a l.*, Bradykinin selectively opens blood-

tumor barrier in experimental brain tumors, J. Cereb. Blood Flow Metab. 14(5):862-70 [1994]). Bradykinin does not increase permeability in the normal blood brain barrier except at very high doses. (Wirth, K. *et al.*, *DesArg9-D-Arg[Hyp3,Thi5,D-Tic7,Oic8]bradykinin (desArg10-[Hoe140]) is a potent bradykinin B1 receptor antagonist*, Eur. J. Pharmacol. 205(2):217-18 [1991]). Opening of the blood-tumor barrier by bradykinin is transient, lasting 15 to 20 minutes. (Inamura *et al.* [1994]). After opening of abnormal brain capillaries with bradykinin, the capillaries become refractory to the bradykinin effect for up to 60 minutes. (Inamura *et al.* [1994]).

Please delete the paragraph at page 19, lines 3-11, and insert therefor the following:

--However, the potassium channel activator employed in the inventive methods is one other than the vasodilator bradykinin (Arg-Pro-Pro-Gly-Phe-Ser-Pro-Phe-Arg)(SEQ ID NO:1), or a polypeptide bradykinin analog, such as receptor mediated permeabilizer (RMP)-7 or A7 (e.g., Kozarich *et al.*, U.S. Patent No. 5,268,164 and PCT Application No. WO 92/18529). Other analogs of bradykinin include related peptide structures which exhibit the same properties as bradykinin but have modified amino acids or peptide extensions on either terminal end of the peptide. Examples of bradykinin analogs include [phe^8 (CH_2–NH) Arg^9-bradykinin, N–acetyl [phe^8 (CH_2--NH--Arg^9] bradykinin and desArg9-bradykinin.--.

In the Claims:

Please amend Claims 1, 17- 24, 48, 64-71, 135-137, 150, and 153, and add new Claims 162-189 as follows.

1.(Twice Amended) A method of delivering a medicant to an abnormal brain region in a mammalian subject, comprising: